

## **REMARKS**

### **I. Status of the Claims**

By this Amendment, claims 2 and 6 have been canceled without prejudice or disclaimer and claims 4 and 7-12 have been canceled without prejudice or disclaimer following their withdrawal from consideration by the Examiner as being directed to non-elected subject matter. Applicants specifically reserve the right to pursue all canceled subject matter in one or more continuation and/or divisional application.

Claims 1, 3, 5 and 13 have been amended without prejudice or disclaimer. New claims 15-20 have been added. Support for the amendments to claims 1 and 5 and the new claims is found throughout the specification, e.g., at page 29, lines 9-18, page 31, lines 3-11 and original claims 2 and 5. The amendments to claims 3 and 13 are not believed to change the scopes of the respective claims.

Upon entry of this Amendment, claims 1, 3, 5 and 13-20 are pending.

By this Amendment, no new matter has been added to the application.

### **II. Interview Summary**

The undersigned attorney conducted a telephonic interview with Examiner Havlin on March 25, 2009, during which time the pending obviousness rejections over U.S. Patent No. 6,342,516 ("the '516 patent") were discussed. The Examiner agreed that compound 37 of the present application (i.e., the elected compound that is specifically claimed in claim 15) was not obvious over compound 3-9 of the '516 patent. More generally, the Examiner indicated that based on the prior art of record it would not have been obvious to substitute an imidazolyl group with a pyrazolyl group to arrive at the compounds of formula (I) and that compounds of formula (I) wherein variable A is pyrazolyl were potentially free of the prior art of record. The Examiner further indicated he would give full consideration to further evidence of unexpected results for compounds of formula (I).

### **III. Claim Objections**

Claims 2, 6, 13 and 14 were objected to as being improper dependent claims because they fail to limit the subject matter of a previous claim. By this Amendment, claims 2 and 6 have been canceled. The objections to claims 2 and 6 are thus moot. Claims 1 and 5 have been amended to include the limitations formerly set forth respectively in claims 2 and 6. Claims 13 and 14 are believed to be proper dependent claims in that they further limit the subject matter of claim 1, from which they each depend. The bases for the instant objections are believed to have been addressed and overcome. Reconsideration of the claims and withdrawal of all objections is requested.

### **IV. Claim Rejections**

The claim rejections set out in the Office Action are summarized and addressed as follows.

*(i) Rejections Under 35 U.S.C. §112, second paragraph.* Claims 1-3, 5, 6, and 14 [sic— claim 13—referring to the phrase “which is substituted at the fourth position on the benzene ring,” which does not appear in claim 14, but which does appear in claim 13] were rejected for alleged indefiniteness. Claims 2 and 6 have been canceled. The rejection, as it pertains to these claims is therefore moot. Claims 1, 3, 5 and 13 have been amended. The claim amendments are believed to address and overcome all issues related to alleged indefiniteness. Reconsideration of the claims and withdrawal of all rejections under section 112, second paragraph is requested.

*(ii) Rejections Under 35 U.S.C. §103.* Claims 1-3, 5, 6, 13 and 14 have been rejected as allegedly obvious over U.S. Patent No. 6,342,516 (“the ‘516 patent”) in view of Patani et al., *Chem. Rev.*, 1996, 96:3147-3176. In setting forth the rejection, the Examiner specifically cites compound 3-9 in Table 3 (columns 59-60) of the ‘516 patent. The rejection is respectfully traversed, as follows.

It is noted at the outset that in their broadest aspect the claims are directed to compounds of formula (I) wherein variable A is either pyrazolyl or imidazolyl. Compound 3-9 of the ‘516 patent is an imidazolyl derivative.

With respect to the case where variable A is pyrazolyl, as set forth above, during the telephonic interview conducted on March 25, 2009, the Examiner agreed that elected compound 37

(claimed in claim 14) was free of prior art and that more generally, based on the current record, subject matter directed to compounds of formula (I) wherein A is pyrazolyl was generally allowable. Accordingly, no further response to the instant rejection is believed to be required as it pertains to compounds of formula (I) wherein A is pyrazolyl.

With respect to compounds of formula (I) wherein A is imidazolyl, the Examiner indicated he would give full consideration to evidence submitted to show compounds of formula (I) wherein A is imidazolyl exhibit unexpected results compared to prior art compounds. Accordingly, submitted herewith is a Declaration Under 37 C.F.R. §1.132 from co-inventor Seiichi Uchida that reports on experiments that demonstrate compounds of formula (I) wherein A is imidazolyl show unexpected results over prior art compounds.

The Declaration provides comparisons of imidazolyl derivatives having an amino group as a substituent G2 on a group of formula (I) (as set forth in claims 1 and 5) with imidazolyl derivatives having a hydroxyl group instead of an amino group (as disclosed in the '516 patent). In particular, the results reported in the Declaration allow a first comparison of the anti-oxidative effects of compound 1 of the present application compared to compound 3-9 of the '516 patent (i.e., the compound cited as the basis for the instant rejection) and a second comparison of the activity of compound 2 of the present application to compound 3-1 of the '516 patent. Compound 1 differs from compound 3-9 of the '516 patent only in that compound 1 has an amino group on the position of the 2,3-dihydrobenzofuran-2-yl group that is occupied by a hydroxyl group in compound 3-9. Similarly, compound 2 differs from compound 3-1 of the '516 patent only in that compound 2 has an amino group on the position of the chromany-2-yl group that is occupied by a hydroxyl group in compound 3-1.

The Declaration reports on the results of experiments designed to compare the anti-oxidative activities of the tested compounds when administered orally to male SD rats at a dose of 100 mg/kg. As reported in the Declaration, the observed inhibition rates of *ex vivo* lipid peroxide action in the brain by compounds 1 and 2 were higher in comparison to the observed inhibition rates for compounds 3-9 and 3-1, respectively. Compared to the respective prior art compounds, compounds 1 and 2 "exhibited significant medicinal benefits even on the brain." See Declaration at page 2.

The effect of replacing the hydroxyl group found on prior art compounds with an amino group, as found in compounds of formula (I), is completely unexpected and could not have been predicted from the prior art. The results reported in the Declaration are thus strong objective evidence that compounds of formula I (as set forth in claims 1 and 5) are not obvious over the prior art of record. All other remaining claims depend from one of either claim 1 or claim 5. Thus, neither are any remaining claims obvious over the prior art of record.

For at least the reasons set forth above, all subsisting claims are believed not to be obvious over the prior art of record. Reconsideration of the claims and withdrawal of all rejections under section 103 is requested.

#### **V. Conclusion**

This application is believed to be in condition for allowance which is earnestly solicited.

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